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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/984,178	12/03/97	HORVITZ	H 01997198006

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EXAMINER	
SHUKLA, R	
ART UNIT	**PAPER NUMBER**
1632	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

5-23-00

Office Action Summary

Application No.	Applicant(s)
08/984,178	Horvitz et al
Examiner	**Group Art Unit**
Ram Shukla	1632

☒ Responsive to communication(s) filed on *Mar 2, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-4, 8-15, 17, 18, 21, and 36* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4, 8-15, 17, 18, 21, and 36* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Amendment filed 3-2-00 (Paper No 12) has been entered.

2. Claims 9-11, 22, 25-27, , 33, 35, and 40 have been canceled.

Claims 1-4, 8, 12-15, 17, 18, 21 and 36 are under consideration in the instant application.

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 8, 15, 17, 18, 21, and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: ced-3 nucleic acid disclosed in Seq ID No 18 or the DNA encoding the amino acid sequence of Seq ID No 19; ced-3 mutants listed in table-3 (see page 62 of the specification) and probes and primers designed on the basis of these sequences, does not reasonably provide enablement for, any and all isolated ced-3 nucleic acids, any and all nucleic acids, probes and primers, structurally related, functionally related or structurally and functionally related to ced-3 nucleic acid sequence of Seq ID NO 18, the RNA encoded thereof, and any and all ced-3 mutants that result from inactivation of ced-3 or constitution inactivation of ced-3 or mutant ced-3 which antagonize the activity of functional cell death genes, for reasons set forth in the previous office action of 8-31-1999. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Amended claim 1 recites an isolated ced-3 nucleic acid wherein the polypeptide encoded by said nucleic acid is hydrophillic in nature and has serine rich region and wherein said nucleic acid can complement ced-3 or ced-4 mutations in in vitro or in vivo assays. Amended claim 8 recites an isolated ced-3 nucleic acid wherein the polypeptide encoded by said nucleic acid is hydrophillic in nature and has serine rich region and comprises a mutation which affects the ability of said ced-3 gene to complement ced-3 or ced-4 mutation in in vivo or in vitro bioassays.

Claim 15 is drawn to an isolated RNA encoded by the nucleic acid of claim 8. Claim 17 recites an isolated nucleic acid comprising: a nucleic acid structurally related, functionally related or structurally and functionally related to ced-3. Claim 18 is drawn to an isolated RNA encoded by the nucleic acid of claim 17. Claim 21 recites a probe or primer for identifying a ced-3 gene family member, nucleic acid comprising consensus sequence of a conserved region between at least two other genes of ced-3 gene family. Claim 36 recites mutant ced-3 mutants that affect the ability to the ced-3 gene to complement ced-3 or ced-4 mutations in in vivo or in vitro bioassays.

As noted in the previous office action, the specification is not enabling for the claimed invention because the specification does not provide sufficient guidance as to how an artisan would have made all the isolated nucleic acids of the ced-3 genes, mutants of ced-3 genes and the probes from all these DNAs encompassed by the claimed invention and would have used these without undue experimentation.

Response to Applicants' Arguments:

Applicants have argued that the claims have been amended to add specific structural and functional limitations to clearly differentiate the ced-3 genes from any and all ced-3 genes. However, these arguments are not deemed persuasive. Applicants have argued that the functional and structural characteristics are applicable to other organisms, for example in mammals, however, there is no such evidence presented in the specification that the ced-3 genes from other organisms will have same or similar characteristics, function or structure, therefore, an artisan would not have been able to make all the ced-3 nucleic acids encompassed by the claimed invention. Applicants argue that the methods to make the family members of the ced-3 gene, based on the functional and structural characteristics are routine, because the specification teaches methods of bioassay and the characteristics of hydrophillicity and the presence of serine rich regions and in vivo or in vitro bioassays (pages 13-17 and 19-21). However, it is noted that while the method to isolated said nucleic acids may be routine, if an artisan does not know whether function, structure or other characteristics of all the claimed nucleic acids may not be same, how would the artisan know how to make and use the nucleic acids. For example, would all the organisms have ced-3 gene or whether their characteristics from all the organisms, for example, from amoeba to mammals or bacteria or plants would be the

same. Would they have the same number of serine residues or same number of hydrophillic motifs or amino acids? Further, would all these nucleic acids function in the bioassays using C.elegans disclosed in the instant application or would the artisan require a bioassay based on the genus of the animal? In other worlds, there is no guidance in the specification as to whether a gene which may have sequence characteristics similar to that of ced-3 gene of C. elegans when added to C.elegans bioassays or in vitro assays would have complemented the function of the mutant ced-3 or ced-4 gene.

Applicants on page 22 argue that the Examiner applied a standard of perfection with respect to enablement that finds no basis in the statute or case law and that if this was the standard, generic claims would never be allowable, however, these arguments are not deemed persuasive. According to the definition provided in the specification (page 13, lines 15-25) structurally related genes refer to genes which have some structural similarity. How much similarity is some similarity? Would a nucleic acid that has 10% sequence similarity over its entire length to another nucleic acid have same or similar function, and the answer is no. Unless the sequences have high sequence similarity, they may not have the same function or even similar function. Next the issue is of functionality. The specification on pages 13 and 14 asserts that the genes encompassing the claimed invention would cause cell death and they can be identified by complimentation in bioassays using ced-3 or ced-4 mutant. However, as disclosed in the specification, cell death can be caused by programmed cell death, deprivation of growth factors, etc., however, without any logical evidence how can one assume that ced-3 would be involved in cell death caused by any reason or by any mechanism. In other words, would any gene which may cause cell death in an organism will be a member of ced-3 gene family, again, there is no evidence in the specification or in the prior art that all genes that would cause cell death would be a member of ced-3 gene family. As noted in the previous office action, just because the claimed DNAs or encoded polypeptides may have some sequence similarity or functional similarity (although, the extent of sequence or functional similarity is not disclosed in the specifications), does not ensure that the resultant DNAs, their encoded polypeptides or mutants thereof would have the same function or even any function as that of the said known protein. Similar arguments are applicable to claims reciting all the mutants or probes or primers encompassed by the claimed invention.

In conclusion, the specification is not enabling for the making and use of any and all isolated ced-3 nucleic acids, any and all nucleic acids, probes and primers of structurally related, functionally related or structurally and functionally related to ced-3 nucleic acid sequence of Seq ID NO 18, the RNA encoded thereof, and any and all ced-3 mutants that result from inactivation of ced-3 or constitution inactivation of ced-3 or mutant ced-3 which antagonize the activity of functional cell death genes and therefor, limitation of the scope of the claimed invention to ced-3 nucleic acid disclosed in Seq ID No 18 or the DNA encoding the amino acid sequence of Seq ID No 19; ced-3 mutants listed in table-3 (see page 62 of the specification) and probes and primers designed on the basis of these sequences, is proper.

5. Claims 1, 8, 15, 17, 18, 21, and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons set forth in the previous office action of 8-31-99.

Applicant is referred to the revised interim guidelines on written description published December 21, 1999 in the Federal Register, Volume 64, Number 244, page 71427-71440 (also available at www.uspto.gov).

Response to Applicants Arguments:

Applicants have argued, both the written description and enablement rejections of 112 first paragraph together and therefore, they have been responded together in paragraph 4 above.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-4, 8, 12-15, 17, 18, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 8, 17, and 21 and their dependent claims are indefinite because they recite "a serine rich region." It is unclear as to how many serines would constitute "a serine rich region", in the absence of any limitations of the number of serine residues, the metes and bounds of the claimed invention are not clear.

Claim Rejections - 35 U.S.C. § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 8, 15, 17, 18, 21, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Yuan (Genetic and Molecular Studies of ced-3 and ced-4: two genes that control programmed cell death in the nematode C.elegans, Thesis presented to Harvard University, Cambridge Massachusetts,1989).

The invention of claims 1, 8, 15, 17, 18, 21, and 36 has been previously described in para 4.

Yuan teaches the cloning of ced-3 in chapter 4 (pages 202-219). This prior art teaches the mapping of ced-3 and limits the ced-3 gene to an interval of two cosmids. Bioassays using cosmids show that the cosmid C48D1 rescued the ced-3 phenotype. This cosmid was further digested with restriction enzymes and fragments were subcloned into and a 14 kb subclone C48D1 still rescued the ced-3 phenotype. This clone was further characterized by digestion and bioassay and finally the subclone C48D1-28 was isolated which still rescued ced-3 (see last paragraph on page 212 and first paragraph on page 213).

Although, Yuan does not teach the hydrophillic nature and serine rich regions of the ced-3 nucleic acid, these would be inherent properties of the ced-3 gene encoded protein.

Therefore, the invention of claim 1, 8, 15, 17, 18, 21, and 36 are anticipated by Yuan.

Response to Applicants Arguments:

Applicants arguments are fully considered, however, they are not deemed persuasive. Although, ced-4 is not recited in the amended claims, since a cosmid clone and two subclones that can complement ced-3 mutant phenotype are disclosed by Yuan, claims reciting ced-3 nucleic acids, or nucleic acid structurally, functionally or structurally and functionally related to ced-3, a probe or primer to identify ced-3 family members are anticipated by Yuan. Further, Yuan, on page 213, states that none of the transformants exhibit complete rescue of the ced-3 mutant phenotype and there are two possible explanations for this result, one a small part of the ced-3 gene may be missing or chromosomal position may be important and that the first possibility can not be excluded. Therefore, the cosmids rescuing partial ced-3 phenotype can be considered as mutants of ced-3 that are inactivated due to lack of certain sequences. In conclusion, all the broad claims that do not recite a particular Seq ID NO are anticipated by Yuan.

10. No claim is allowed.

11. Claims 2-4 and 12-14 are free of prior art.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Thursday and every other Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached on (703) 308-2035. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 305-0196.

Ram R. Shukla, Ph.D.

Jasemine C. Chambers

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